AMENDMENT

IN THE CLAIMS

Please enter the following amendments to the claims without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents as follows:

1. (Original) A transgenic non-human animal to which a regucalcin gene is introduced and which overexpresses regucalcin.

2. (Currently amended) The transgenic non-human animal according to claim 1, wherein straight chain DNA which is arranged in the order of cytomegalovirus-IE enhancer, chicken β-actin promoter, regucalcin gene, rabbit ~~β-glovin~~ β-globin poly A signal is introduced.

3. (Original) The transgenic non-human animal according to claim 1, wherein the regulcaltin gene is a gene that encodes protein consisting of amino acid sequence of Seq. ID No.2 of the sequence listing.

4. (Original) The transgenic non-human animal according to claim 3, wherein the gene encoding protein consisting of amino acid sequence of Seq. ID No.2 of the sequence listing is, a rat regucalcin gene consisting of DNA sequence of Seq. ID No.1 of the sequence listing.

5. (Original) The transgenic non-human animal according to claim 1, wherein the animal is homozygote.

6. (Original) The transgenic non-human animal according to claim 1, wherein the animal has an ability to suppress the weight gain.

7. (Original) The transgenic non-human animal according to claim 1, wherein the animal is susceptible to dysfunction of cerebrum.

8. (Original) The transgenic non-human animal according to claim 1, wherein the animal is susceptible to insulin independent diabetes.

9. (Original) The transgenic non-human animal according to claim 1, wherein the animal is susceptible to renal hypertension.

10. (Original) The transgenic non-human animal according to claim 1, wherein the animal is susceptible to impairment of tubular reabsorption.

11. (Original) The transgenic non-human animal according to claim 1, wherein the non-human animal is a rat.

12. (Original) A method for producing regucalcin, wherein the transgenic non-human animal according to claim 1 is used.

13. (Original) A screening method of preventive and therapeutic agents for diseases caused by the overexpression of regucalcin, wherein the transgenic non-human animal according to claim 1, or tissues, organs or cells derived from the transgenic non-human animal and a test substance are used.

14. (Original) The screening method of preventive and therapeutic agents for diseases caused by the overexpression of regucalcin according to claim 13, wherein the test substance is administered to the transgenic non-human animal, and the level of the weight gain of said transgenic non-human animal is measured and estimated.

15. (Original) The screening method of preventive and therapeutic agents for diseases caused by the overexpression of regucalcin according to claim 13, wherein the disease caused by the overexpression of regucalcin is dysfunction of cerebrum.

16. (Original) The screening method of preventive and therapeutic agents for diseases caused by the overexpression of regucalcin according to claim 13, wherein the disease caused by the overexpression of regucalcin is insulin independent diabetes.

17. (Original) The screening method of preventive and therapeutic agents for diseases caused by the overexpression of regucalcin according to claim 13, wherein the disease caused by the overexpression of regucalcin is renal hypertension.

18. (Original) The screening method of preventive and therapeutic agents for diseases caused by the overexpression of regucalcin according to claim 13, wherein the disease caused by the overexpression of regucalcin is impairment of tubular reabsorption.

19. (Original) A preventive or therapeutic agent for diseases caused by the overexpression of regucalcin obtained by the screening method according to claim 13.

20. (Original) A screening method of causative agents of diseases caused by the lowering of regucalcin expression wherein the transgenic non-human animal according to claim 1, or tissues, organs or cells derived from the transgenic non-human animal and a test substance are used.

21. (Original) The screening method of causative agents of diseases caused by the lowering of regucalcin expression according to claim 20, wherein the test substance is administered to the transgenic non-human animal, and the level of the weight loss of the transgenic non-human animal is measured and estimated.

22. (Original) The screening method of causative agents of diseases caused by the lowering of regucalcin expression according to claim 20, wherein the disease caused by the lowering of regucalcin expression is arteriosclerosis myocardial infarction.

23. (Original) The screening method of causative agents of diseases caused by the lowering of regucalcin expression according to claim 20, wherein the disease caused by the lowering of regucalcin expression is myocardial infarction.

24. (Original) A causing substrate of disease caused by the lowering of regucalcin expression obtained by the screening method according to claim 20.

25. (Original) An animal model having bone pathology wherein the animal model is a non-human animal that overexpresses regucalcin and shows bone pathology.

26. (Original) The animal model having bone pathology according to claim 25, wherein the animal expresses one or more bone pathology of any of vulnerability of bone tissue, change of bone morphology or delay in bone growth.

27. (Original) The animal model having bone pathology according to claim 25, wherein the animal is selected and determined among non-human animal that overexpresses regucalcin by a morphological measurement estimation of bone and/or a biochemical measurement estimation of bone component.

28. (Original) The animal model having bone pathology according to claim 27, wherein the morphological measurement estimation of bone is one or more measurement estimations of any of bone density, bone strength, bone thickness of diaphyseal cortex or length of surrounding of cortex.

29. (Original) The animal model having bone pathology according to claim 27, wherein the biochemical measurement estimation of bone component is one or more measurement estimations of any of amount of calcium, alkaline phosphatase activity or amount of DNA in bone tissues.

30. (Original) The animal model having bone pathology according to any of claims 25, wherein the characteristic of bone pathology is stable through many generations.

31. (Original) The animal model having bone pathology according to claim 25, wherein the non-human animal that overexpresses regucalcin is a transgenic non-human animal to which regucalcin gene is introduced.

32. (Original) The animal model having bone pathology according to claim 26, wherein the non-human animal that overexpresses regucalcin is homozygote.

33. (Currently amended) The animal model having bone pathology according to ~~any of claims~~ claim 31, wherein the non-human animal that overexpresses regucalcin is a female non-animal.

34. (Cancel)

35. (Original) The animal model having bone pathology according to claim 25, wherein the non-human animal that overexpresses regucalcin is a rat.

36. (Original) A screening method of preventive and therapeutic agents for bone diseases wherein a test substance is administered to a animal model having bone pathology according to claim 25, and a morphological measurement estimation of bone and/or a biochemical measurement estimation of bone component of said animal model having bone pathology are performed.

37. (Original) The screening method of preventive and therapeutic agents for bone disease according to claim 36, wherein the morphological measurement estimation of bone is one or more measurement estimations of any of bone density, bone strength, bone thickness of diaphyseal cortex or length of surrounding of cortex.

38. (Original) The screening method of preventive and therapeutic agents for bone disease according to claim 36, wherein the biochemical measurement estimation of bone component is one or more measurement estimations of any of amount of calcium, alkaline phosphatase activity or amount of DNA in bone tissues.

39. (Original) The screening method of preventive and therapeutic agents for bone disease according to claim 36, wherein the bone disease is aosteoporosis.

40. (Original) A preventive or therapeutic agent for bone disease obtained by the screening method according to any of claims 36.